



FIG. 1

PH: domain 1 of 2, from 507 to 620: score 65.9, E = 4.1e-17

```
*->vikeGwLlkks.....kswkkRyfvLfnnvLlyykds
  v + GwL+ k   + +++++ +   +++wk+++++L++ +Ll+y+
33521  507  VRRAGWLFFKPlvtvqkerklelvarRKWKQYWVTLKGCTLLFYETY 553

      k.....kpkgsipLsgcqvek.pd....kncFeirt.dr.tlllqae
      ++++ +++++ p+  + +++++v  p++++++n+F+++++ +++++l+qa+
33521  554  GknsmdqsSAPRCALFAEDSIVQSVPEhpkkENVFCLSNsFGdVYLFQAT 603

      seeerkeWvkaiqsair<-* (SEQ ID NO:4)
      s+ +++ Wv+a +sa++
33521  604  SQTDLNWWVTAVHSACA      620
```

FIG. 2A

RBD: domain 1 of 1, from 810 to 873: score -3.0, E = 2.3

```

      *->ktirvhLPnnqrsVvevRpGmtvrDaLakalkkRGLnpsacvVrrsg
            +   vh  +n  ++V  +p  +v+D+L  a+k+R+L  ps   +
33521  810  IQTYVHFQDNHGVTVGIKPEHRVEDILT LACKMRQLEPSHYGLQ--- 853

      dpqeGekkpLdltdissLpgPeElvvEnl<-* (SEQ ID NO:5)
            L+ d + + +p+P   +E
33521  854  -----LRKLVDNVEYCIPAP----YEYM      873
```

FIG. 2B

PDZ: domain 1 of 1, from 890 to 975: score 33.5, E = 4.8e-06

```

      *->eitlekevkr gglGfsikggsdk.....givvsevlpGsgaAeagGr
      +++l k + +Gf + + d++++ + i++s+vlp+ g A G
33521 890 DVQLTKTGSVCDFGFAVTAQVDErghlsRIFISDVLPD-GLAYGEG- 934

      LkeGDvIlsvNGqdvenms heravlaikgsgg.evtLtvIRd<-* (SEQ ID NO:6)
      L++G I+ NG+ v+++ ++++++a+ + ++ +tL +++
33521 935 LRKGNEIMTLNGEAVSDL-DLKQMEALFSEKSvGLTLIARPP 975

```

FIG. 2C

33521 1103 1144 1191 1237 1278 1292

RhoGEF: domain 1 of 1, from 1103 to 1292: score 147.0, E = 3.3e-40
*->vlkElleTEkkYvrdLeildnvymkpLreaaisskpvltpddietif
v+ El+ TEk Yv+dL l y++pL+++ +lt+d++e++F
33521 1103 VIQELVDTEKSYVKDLSCLFELYLEPLQNET-----FLTQDEMESLF 1144

sNiediyefhreFLkssLearisssqfedlDe....kkiepsaprlGdlF
+ +++ +ef++ FL Le+ is+s d + +++ + lG F
33521 1145 GSLPEMLEFQKVFL E-TLEDGISAS--SDFNTletpSQFRKLLFSLGGSF 1191

lklkepflqvYgeYcsnkpyAgelleklrqaasnpqFaefldeveassnt
l + ++ +++Y +c+n+ +q++le+ a++ +F+ fld + + +
33521 1192 LYY-ADHFKLYSGFCANHIKVQKVLER---AKTDKAFKAFLDARNPTKQH 1237

gAkddavkltLqsLLlkPvqRilrYpLLLkeLLkhtpegedqpdredLkk
tL+s+L+kPvqR+l+YpLLLkeL+++t+ +++++ L +
33521 1238 S-----STLESYLIKPVQRVLKYPLLLKELVSLTDQ--ESEEHYHLTE 1278

aldllqdlaksiNe<-(SEQ ID NO:7)
al++++ +a++iNe
33521 1279 ALKAMEKVASHINE 1292

FIG. 2D

PH: domain 2 of 2, from 1353 to 1455: score 4.3, E = 8.7

```
*->fvLfnnvLlykdsk.....kkpkgsipLsg
      fv+++ v+l yk+  + +++ ++++++ ++++++ +++k +  ip+s
33521  1353  FVFKRAVILVYKENcklkkklpsnsrpahnstdldpFKFRWLIPISA 1399

      cqvek.pd.....kncFeirt.dr.....tlllqaeseeerkeWvka
      +qv+ +  +++++ +e++++ + ++++++ + l+++++e++  vk
33521  1400  LQVRLgNPagtenNSIWELIHtKSeiegrpetIFQLCCSDSESKTNIVKV 1449

      iqsair<-* (SEQ ID NO:8)
      i+s++r
33521  1450  IRSILR      1455
```

FIG. 2E

PH_update: domain 1 of 2, from 507 to 622: score 63.3, E = 5.2e-15

```

      *->vikeGwLlkks.....k.swkkryfvLfngvLllyksk
      v + GwL  k   + ++ ++      +++wk+++++L++ +Ll+y+
33521  507  VRRAGWLFFKPlvtvqkerklelvaRrKWKQYWVTLKGCTLLFYETY 553

      .....kpkgsipLsgcsvre.p.....cFeivt.dr.tlllqAe
      ++++ ++++p+  ++ ++ +v+  p+++++++F+++++ ++++l+qA
33521  554  gknsmdqssAPRCALFAEDSIVQSvPehpkkenVFCLSNsFGdVYLFQAT 603

      seeereeWvealqsaiaka<-* (SEQ ID NO:9)
      s+ ++e Wv+a +sa+a++
33521  604  SQTDLNwVTVAVHSACASL      622

```

FIG. 3A

RBD_5: domain 1 of 1, from 810 to 881: score 68.6, E = 1.3e-16
 *->ktervhLPdnqrtvVkvRPGktvrDaLakaLkkRgLnpeacvVrlrg
 ++++vh++dn +++V ++P+++v+D+L +a+k+R+L+p+++++lr+
 33521 810 IQTYVHFQDNHGVTVGIKPEHRVEDILT LACKMRQLEPSHYGLQLRK 856
 dpqeGekkpdlndissLagqElvveel<-* (SEQ ID NO:10)
 ++ ++ + ++ +++++q +v++e+
 33521 857 L----VDDNVEYCI PAPYEYMQQVYDEI 881

FIG. 3B

pdz_new: domain 1 of 1, from 900 to 976: score 39.3, E = 8.9e-08

```

      *->gglGfsivg.....gifvssvvpGspAakaGrkslgllKvGDv
          +Gf ++ + +++++ + if+s+v+p++ A+  G      L++G +
33521   900   CDFGFAVTAqvderqhlsRIFISDVLPDGLAYGEG-----LRKGNE 940

          IleVNGetsvegltheeavdllkkaggggvGekvtLtlvRgg<-* (SEQ ID NO:11)
          I+  NG + v++l+  +  +l  +  +      +tL+ +++++
33521   941  IMTLNG-EAVSDLDLKQMEALFSEKSV-----GLTLIARPPD    976

```

FIG. 3C

33521 1103 1143 1189 1233 1277 1292

RhoGEF_3: domain 1 of 1, from 1103 to 1292: score 217.7, E = 1.8e-61
 *->vIkELlqTErnYVrdLkIlvevflkpLkkeakssllpllsPdevktl
 v++EL++TE++YV+dL +l e +l+pL++e +l++de+++l
 33521 1103 VIQELVDTEKSYVKDLSCLFELYLEPLQNET-----FLTQDEMESL 1143
 FgpNieeiYefHrrFLdeLeerveewllskdl.Ksernsviedsgerigd
 Fg ++e +ef++ FL++Le+ ++ + d++ e+ s++++ +g
 33521 1144 FG-SLPemLEfQKVfLETLEDGISASS---DFnTLETpSQFRKLLfSLGG 1189
 vFlklfsaeeffkiYseYcsnhpdalellkkLmkkkknpaFqkflkeies
 Fl + +++fk+Ys +c+nh + +++l+ +k+++aF++fl+ +
 33521 1190 SFLYY---ADHFKLYSGFCANHIKVQKVLER---AKTDKAFKAFLDARNP 1233
 kpncrsksearltLeslLikPvQRltkYpLLLkellkhtppdhedredLk
 ++++ tLes+LikPvQR++kYpLLLkel t+ ++e++ +L+
 33521 1234 TKQHS-----STLESYLIKPVQRVLKYPLLLKELVSLTDQEEHYHLT 1277
 kAleaikelasqvNe<-* (SEQ ID NO:12)
 +Al+a++++as++Ne
 33521 1278 EALKAMEKVASHINE 1292

FIG. 3D

PH_update: domain 2 of 2, from 1326 to 1457: score 17.7, E = 0.28

```

      *->vikeGwLlkks.....k.swkkryfvLfngvLlyyysk.....
          +++++ +++++ + + ++ ++          fv+++ v+l yk+ + +++
33521  1326  LLMHSTVSWLNpflslgkaRkDLELTVFVFKRAVILVYKENcklkkk 1372

          .....kpkgsipLsgcsvre.p.....cFeivt.d
          +++++ +++++ ++ k +  ip+s ++vr + + + +++++ +e+++++
33521  1373  lpsnsrpahnstdldpfKFRWLIPISALQVRLgNpagtennsIWELIHtK 1422

          r.....tlllqAeseeereewvealqsaiaka<-* (SEQ ID NO:13)
          + ++++++ + l+++++e+++  v+ ++s ++++
33521  1423  SeiegrpetIFQLCCSDSESKTNIVKVIRSILREN      1457

```

FIG. 3E